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10/666,998	09/19/2003	Andrei Laikhter	013670-9004 US00	1003
53229 7590 09/17/2009 MICHAEL BEST & FRIEDRICH LLP ONE SOUTH PINCKNEY STREET P.O. BOX 1806 MADISON, WI 53701				
EXAMINER				
STAPLES, MARK				
ART UNIT		PAPER NUMBER		
1637				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/666,998

**Applicant(s)**

LAIKHTER ET AL.

**Examiner**

MARK STAPLES

**Art Unit**

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 May 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 51-61 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 51-61 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SG/US)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Applicant's cancellation of claims 1-50 and the submission of new claims 51-61 in the paper filed on 05/20/2009 is acknowledged. The amendment to the specification is acknowledged.

Claims 51-60 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### **Objection and Rejections that are Moot / Withdrawn**

##### ***Canceled Claim Objections and Rejections Moot / Withdrawn***

2. The objection and/or rejections of canceled claims 37-50 are moot and therefore are withdrawn.

#### **New Objections and Rejections Necessitated by Amendment**

##### ***New Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 51-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Batz et al. (United States Patent No. 6,117,973 issued September 12, 2000, previously cited).

Regarding claims 51 and 53, Batz et al. teach methods of detecting a target nucleic acid sequence which is DNA in a sample (see column 21 lines 42-63 and Example 11), comprising:

contacting the sample with an oligonucleotide specific for hybridizing to the target sequence labeled with a fluorophore and a quencher, and wherein fluorescence of the fluorophore which is an acridine moiety can be reduced by energy transfer to the quencher or by ground state quenching by the quencher which is an anthraquinone moiety (see Example 11, especially column 36 lines 17-49 with SEQ ID NO: 3 which is the labeled PNA626 oligonucleotide; and wherein the quencher moiety can be an  $\alpha$ -aminoanthraquinone according to formula VIa (see claim 7) where:

$$n = m = 0;$$

$$(R)_1 = \text{hydrogen};$$

$$(R)_k = N(R''R') \text{ in an } \alpha \text{ position};$$

$$R' = OR';$$

$$R' = PO_3^{2-} \text{ or } PO_2^-; \text{ and}$$

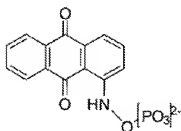
$R''$  is any of the groups other than acetyl that can covalently bind to nitrogen (as listed in claim 7).

and specifically further teaches the  $\alpha$ -aminoanthraquinones where:

$$R_1 = R_{14} = R_{15} = R_6 = R_7 = R_8 = R_9 = R_{10} = \text{hydrogen};$$

$$R_1 = R_{14} = R_{15} = \text{hydrogen}; \text{ and}$$

X =  $\text{PO}_3^{2-}$  (a first  $\alpha$ -aminoanthraquinone given below) or =  $\text{PO}_2^-$  (a second  $\alpha$ -aminoanthraquinone);



; and

detecting a change in fluorescence (see column 21 lines 42-63).

Regarding claims 52 and 55, Batz et al. teach  $\alpha$ -alkylaminoanthraquinones and  $\alpha$ -arylaminoanthraquinones including di- $\alpha$ -alkylaminoanthraquinones and di- $\alpha$ -arylaminoanthraquinones according to formula VIa (see claim 7) as given above, but where:

$(R)_1 = (R)_k = \text{N}(R''R')$ , each in an  $\alpha$  position;

$R_1 = R_{14} = R_{15} = R_6 = R_7 = R_8 = R_9 = R_{10} = \text{hydrogen}$ ;

$R_1 = R_{14} = R_{15} = \text{hydrogen}$ ; and

$R' = \text{hydrogen}$ ;

$R''$  is in each case is an alkyl or a fused aryl (as listed in claim 7).

Regarding claim 54, Batz et al. teaches di- $\alpha$ -aminoanthraquinones according to according to formula VIa (see claim 7) as given above but where  $(R)_1 = N(R''R')$  also is an  $\alpha$  position and specifically teaches the di- $\alpha$ -aminoanthraquinones where:

$(R)_1 = (R)_k = N(R''R')$ , each in an  $\alpha$  position;

$R_1 = R_{14} = R_{15} = R_6 = R_7 = R_8 = R_9 = R_{10} = \text{hydrogen}$ ;

$R_1 = R_{14} = R_{15} = \text{hydrogen}$ ; and

$X = \text{PO}_3^{2-}$  (a first di- $\alpha$ -aminoanthraquinone given below) or  $= \text{PO}_2^-$  (a second di- $\alpha$ -aminoanthraquinone).

Regarding claim 56, Batz et al. teaches where the fluorescence is reduced by fluorescent energy transfer (see column 36 lines 5-6).

Regarding claim 57, Batz et al. teaches where the fluorescence is reduced by ground state quenching (see column 4 lines 37-53).

Regarding claim 58, Batz et al. teaches where the fluorescence is reduced by fluorescent energy transfer (see column 36 lines 5-6) and where the fluorescence is reduced by ground state quenching (see column 4 lines 37 to column 5 line 46 for a process where both excited state of fluorescent energy transfer occurs and ground state follows with the reduced fluorescence of donor and acceptor/quencher complex).

Regarding claim 59, Batz et al. teaches a decrease in fluorescence when the hairpin probe is in the folded configuration (see Example 11, especially Table 3).

Regarding claim 60, Batz et al. teaches an increase in fluorescence when the hairpin probe is in the unfolded configuration (see Example 11, especially Table 3).

*Applicant's Arguments regarding Batz et al.*

It is noted that Batz et al. teach the limitations of the newly submitted method claims and thus that these teachings anticipate the claims, as given above. Thus and although argued by Applicant, no reason need be given for the prior art disclosure by Batz et al. of using the claimed various  $\alpha$ -aminoanthraquinones in the claimed methods. Applicant further argues that Batz et al. does not disclose certain properties of the  $\alpha$ -aminoanthraquinones. Examiner disagrees as noted above. Regardless the properties are inherent to the  $\alpha$ -aminoanthraquinones, and as Batz et al. teach the  $\alpha$ -aminoanthraquinones in the methods as recited in the instant claims, the methods of the Batz et al. using the  $\alpha$ -aminoanthraquinones with their inherent properties anticipate the instant claims.

5. Claim 61 is rejected under 35 U.S.C. 103(a) as being unpatentable over Batz et al. as applied to claim 37 above, and further in view of Jenne et al. (United States Patent No. 6,451,535 issued September 17, 2002, previously cited).

Batz et al. teach as noted above.

Batz et al. do not specifically teach separation of an anthraquinone quencher from a fluorophore by cleaving an RNase restriction site between them.

Regarding claims 61, Jenne et al. teach wherein the system is a system for measuring RNase activity, wherein the nucleic acid polymer is a ribonucleic acid polymer comprising the fluorophore attached thereto, wherein the ribonucleic acid polymer comprises an RNase restriction site between the quencher and the fluorophore, a change in fluorescence indicating the presence of RNase which is ribonuclease P (see Figure 1 and see column 2 lines 32-40).

Jenne et al. do not teach an anthraquinone quencher.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Jenne et al. by substituting an anthraquinone quencher as suggested by Batz et al. with a reasonable expectation of success. The motivation to do so is provided by Batz et al. who teach that anthraquinones are preferred acceptors/quenchers in quencher and fluorophore pairs (see column 15 line 44) and the teaching of Jenne et al. that quencher and fluorophore pairs can be used to monitor RNase activity (entire patent, especially Figures 1-4 and see column 2 lines 32-40) for direct, reproducible, highly sensitive, and simple detection of mRNA in cell extracts (see column 2 lines 1-19). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.



**Conclusion**

6. No claim is allowed.
7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples  
/M. S./  
Examiner, Art Unit 1637  
September 14, 2009

/GARY BENZION/  
Supervisory Patent Examiner, Art Unit 1637